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Clinical and Morphological Substantiation of the Choice of Treatment Method for Diabetic Foot Syndrome

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ABSTRACT

Background. Usually, in clinical practice, only the external characteristics of the forming granulation tissue are evaluated, which is insufficient and can lead to errors in treatment. The morphological characteristics of granulation maturity were evaluated in laboratory models or individuals without carbohydrate metabolism disorders.

Methods. The study was conducted in the design of an open prospective, randomized comparative study with parallel groups, including patients with diabetes mellitus and diabetic foot syndrome. General clinical, biochemical, instrumental, functional, morphological, immunological, histochemical, and statistical research methods were carried out.

Results. Modern methods of local treatment after primary surgical treatment of chronic wounds should be used differentially depending on the volume of the wound and the amount of exudate. This will significantly improve the therapeutic prognosis and shorten the duration of treatment. The optimization of the treatment process was noted, and the period of stay of the patient in the hospital was significantly reduced. The intensity of reparative processes can be assessed by determining immunohistochemical markers such as CD31, CD68, osteopontin, activity of matrix metalloproteases, and tissue inhibitor of metalloproteases. As a reliable predictor of good wound healing, there is an increase in local microhemodynamics according to transcutaneous oximetry.

Conclusions. Reparative processes in the soft tissues of the lower extremities are impaired in individuals with diabetes mellitus. Different types of local treatment of wounds have different effects on the intensity of healing processes in patients with diabetes mellitus. The type of topical treatment may affect local microhemodynamics in the tissues surrounding the wound.

Keywords: Diabetes mellitus, diabetic foot syndrome, wound regeneration

INTRODUCTION

Diabetes mellitus is one of the most important medical and social problems. According to data provided by the International Diabetes Federation, the number of people suffering from this disease in the world is 382 million people [4].

In 30-80% of patients with diabetes mellitus, chronic wound defects of the soft tissues of the lower extremities of various origins are recorded [14]. In more than half of the cases, the course of the wound process in persons with this pathology is extremely long and may be accompanied by the addition of wound infection and pain syndrome [9]. Wounds can be resistant to treatment, which leads to a decrease in the quality of life of patients and poses an immediate risk of subsequent amputation [1]. Even in the case when radical surgical intervention

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can be avoided, long-term and extremely expensive treatment of trophic disorders of the soft tissues of the lower extremities leads to huge costs of both material resources and time of medical personnel [11].

Usually, in clinical practice, only the external characteristics of the emerging granulation tissue are evaluated, which is insufficient and can lead to errors in treatment. Morphological characteristics of granulation maturity were evaluated in laboratory models or individuals without carbohydrate metabolism disorders. To date, such indicators of the viability of granulation tissue as the rate of neovasculogenic, proteolytic activity, and the number of macrophages, as the main source of growth factors necessary for healing, remain poorly understood.

Normally, wound healing includes several sequential biological and molecular processes that begin with the migration and proliferation of cells in damage and rearrangement of the extracellular matrix and end with the remodeling of newly formed tissues and blood vessels [5]. Effective repair is not possible without a timely and accurate cellular response, which consists of the activation of keratinocytes, fibroblasts, endothelial cells, macrophages, and platelets, which synthesize various growth factors and cytokines that regulate the wound process and lead to the achievement of epithelialization [16].

It is believed that with long-term and poorly controlled diabetes mellitus, due to the development of late micro- and macrovascular complications, the expression of local growth factors decreases [17].

Currently, numerous studies are being conducted on the role of cytokines, and growth factors in wound healing in diabetes mellitus, but there is still no unified assessment of the role of these molecules in repair [21].

Hyperglycemia leads to impaired immune responses, which significantly increases the risk of secondary infection. The glycation of proteins changes their structure and function, which plays an important role in the development of microvascular complications of diabetes mellitus [3].

According to experimental studies, a high concentration of glucose inhibits the proliferation of human fibroblasts in cell culture, bovine endothelial cells, and primary keratinocytes of mouse skin. Fibroblasts lose sensitivity to stimulation by growth factors, and human endothelial cells and macrophages begin to produce a greater number of molecules of average weight [8].

Chronic wound defects in diabetes mellitus are in the phase of inflammation for a longer period than with normal carbohydrate metabolism, there is reduced activity of inflammatory cells and a slowdown in the restructuring of the extracellular matrix. The above disorders contribute to the transformation of the wound from acute to chronic [2].

The most informative indicators of the intensity of repair in soft tissues are the vascular endothelial marker (CD 31 antibody), the activity of matrix metalloproteases (MMP-9) and tissue metalloprotease inhibitor (TIMP-1), the macrophage marker (CD68), and the matrix cell protein osteopontin [13,19].

In this regard, it seems appropriate to study the features of changes in these indicators reflecting tissue repair against the background of various methods of local treatment in individuals with diabetes mellitus.

MATERIALS AND METHODS

The study was carried out in the design of an open prospective randomized comparative study with parallel groups, which included patients with diabetes mellitus and diabetic foot syndrome who were hospitalized in a multidisciplinary clinic of the Tashkent Medical Academy in the period 2018-2022. Patients were assigned to local treatment groups by random sampling.

63 patients with type 1 and type 2 diabetes mellitus with neuropathic and neuro-ischemic forms of diabetic foot syndrome (without critical ischemia of the lower limb) aged 32 to 78 years were examined. All patients underwent surgical treatment of the wound defect of the lower limb (traditional or hydro surgical system Versa Jet, Smith & Nephew, UK) with excision of necrotic tissues and sanitation of the focus of infection, after which a biopsy of the wound defect was taken for histological and immunohistochemical examination. As a biopsy material, a section of tissue was taken from the centre of the wound, with a volume of about 0.5 sm3.

After surgical debridement of the wound, the patients were divided into groups by random sampling. The first group consisted of patients who received negative pressure therapy ranging from -90 to -120 mm Hg as a local treatment. (VivanoTec, Hartmann. Germany; Renasys, Renasys Go, Smith &Nephew. Great Britain), the change of the sponge dressing was carried out 1 time in 3-4 days, depending on the local status and severity of exudation. The second group included patients who were on therapy with collagen-containing dressings Promogran (Systagenix, UK), dressing was carried out 1 time in 2 days, according to the recommendations for the use of this dressing. The third group, the control group, included patients who received standard treatment with atraumatic dressings (Adaptic, Systagenix, UK; Atrauman,

Hartmann, Germany). Given the low absorbency of the above closures, such dressings as Mesorb (Molnlycke Health Care, Sweden), and Zetuvit (Hartmann, Germany) were used as secondary dressings. The dressing was changed daily. Groups 1 and 2 were not compared with each other due to the different mechanisms of action of the studied methods (the physical method of exposure to vacuum therapy and the competitive interaction of bovine collagen, which is part of collagen-containing dressings, with matrix metalloproteases of the wound environment). In addition, according to international guidelines for the treatment of diabetic foot syndrome the use of negative pressure and collagen refers to adjuvant treatments, as opposed to standard topical treatment with atraumatic dressings.

The examination included examination, analysis of clinical and anamnestic data, and results of laboratory and instrumental, histological and immunohistochemical studies. During the hospital stay, all patients underwent unloading of the lower extremities, according to indications, antibiotic therapy was carried out. Antibacterial drugs were prescribed to prevent secondary infection of wounds, which is possible when changing dressings. During hospitalization, all patients had glycemic values within the individual target values.

All patients signed an informed consent to a particular method of treatment. The study protocol was approved at a meeting of the ethics committee of the Ministry of Health of the Republic of Uzbekistan dated September 15, 2017 (protocol # 23).

A general clinical blood test was performed on a haematology analyzer XE 2100 (Sysmex, Japan) with automatic loading of samples. A biochemical blood test was performed on an automatic biochemical analyzer Architect plus C 4000 (Abbott Diagnostics, USA) by the photometric method according to standard methods using the manufacturer's reagents. The level of glycated haemoglobin was determined by high-performance high-pressure liquid chromatography on the D-10 apparatus (BioRad Laboratories, USA) according to the manufacturer's standard methodology.

All laboratory tests of blood samples were carried out according to standard methods based on the clinical diagnostic laboratory of the medical and biological laboratory of the Tashkent Medical Academy.

Tactile sensitivity was assessed using a monofilament weighing 10 g (North Coast Medical Inc., USA) according to the standard method. Vibration sensitivity was determined using a graduated 128 Hz tuning fork (Kircher & Wilhelm, Germany) on the tibial tubercle and on the medial surface of the head of the 1st metatarsal bone. The state of temperature sensitivity was determined using the Tip-Therm device (Neue Medizintechnik Gmbh, Germany). The severity of pain was assessed using a 5-point verbal pain assessment scale.

The area of the wound was determined by the planimetric method by delineating the contours of the wound through a transparent scale film (Opsite Flexgrid, Smith and Nephew, UK), followed by counting the number of square sm inside the contour. The depth of the wound defect was assessed using a sterile ruler.

Blood flow through the dorsal arteries of the foot, anterior and posterior tibial arteries, as well as the state of venous outflow were assessed based on the results of duplex scanning on the Voluson 730 apparatus (General Electric, USA). Determination of transcutaneous oxygenation of the skin of the near-wound zone (tpO2) was carried out by transcutaneous oximetry. To measure tcpO2, an oximeter "TSM-30" (Radiometer, Denmark) was used.

Morphological analysis of the material included histological and immunohistochemical research methods. The biopsy material was fixed in a 10% formalin solution and then poured into paraffin according to the standard method. Serial sections with a thickness of 3 μm were dewaxed according to the standard scheme and stained with hematoxylin and eosin.

The assessment of the severity of edema and extracellular matrix was carried out by a semi-quantitative method using a point assessment, where 1 "+" is weakly expressed, 2 "+" is moderately pronounced, 3 "+" is strongly pronounced, 4 "+" is very strongly pronounced.

The maturity of the granulation tissue was assessed by determining the area of necrosis, the number of vessels, the severity of the inflammatory infiltrate and the cellular composition (polymorphonuclear leukocytes, lymphocytes, macrophages, fibroblasts), and was divided into young, granulation tissue: connective tissue rich in cells and thin-walled vessels, between the vessels there are many undifferentiated lymphocyte-like cells of connective tissue, leukocytes, plasma cells and labrocytes, 2 – maturing granulation tissue: differentiation of cellular elements, fibrous structures, as well as blood vessels continues. The number of hematogenous elements decreases, and fibroblasts increase. In connection with the synthesis of collagen fibroblasts in the intercellular spaces, argyrophilic and then collagen fibres are formed. As fibroblasts mature, the number of collagen fibers increases, they are grouped into bundles; 3 – mature granulation tissue: fibrous connective tissue.

The phases of inflammation were determined based on the standard classification, where phase 1 is inflammation: neutrophilic granulocytes, monocytes and macrophages predominate in the wound, phase 2 is the regeneration and maturation of granulation tissue: the latter is formed in the form of separate foci at the bottom of the wound and is characterized by an intense neoplasm of capillaries. Many fibroblasts are determined, the formation of collagen and elastin fibers, phase 3 - scarring and epithelialization: maturing, mature, where 1 - young granulation tissue turns into mature fibrous tissue with coarse collagen fibers and fibrocytes.

An immunohistochemical study was performed on the immunostained Leica BOND-MAX (Germany). Antibodies to tissue metalloproteinase inhibitor 1 (TIMP-1), matrix metalloprotease 9 (MMP-9), CD68 antibody (a protein of the lysosomal glycoprotein family expressed by macrophages, monocytes, neutrophils, basophils, and NK cells), platelet and endothelial cell adhesion molecule -1 CD31 and osteopontin protein were used.

Evaluation of the expression of cytoplasmic markers such as TIMP-1, MMP-9, osteopontin was carried out by a semi-quantitative method: 1 "+" staining of single cells (less than 30% of cells), 2 "+" - 30-60% of cells, 3 "+" - 60-90%, 4 "+" - more than 90% of cells.

The degree of expression of CD68 (a marker of histiocytic cells) was calculated by a semi-quantitative method based on the number of immunopositive cells and varied in the ranges: 5-10%, 10-15%, 15-20%, 20-30%, 30-40% of specifically stained cells.

The density of vessels per unit area (0.75mm2 [magnification 20s, lens field of view diameter 1 mm]) was estimated by counting the number of vessels whose endothelium expressed CD31 at the place of their greatest density.

Morphologists were not informed of the method of local treatment in the examined patients, thus, histological and immunohistochemical examination were blinded.

Statistical processing of the obtained data was carried out using the STATISTICA application package (StatSoft Inc., USA, version 6.0). To analyze the type of distributions, the Shapiro-Wilk and Lilliefors criteria were used, and the variances of the feature distributions were estimated using the F-test in the ANOVA analysis of variance procedure. Given the small sample sizes and distributions different from normal, nonparametric methods of data analysis were used. Comparison of independent groups by quantitative characteristics was carried out by a nonparametric method using the Mann-Whitney U-test. Comparison of dependent groups by quantitative characteristics was carried out by a nonparametric method using the Wilcoxon test. Comparison of independent groups by qualitative characteristics was carried out by a nonparametric method by analyzing contingency tables using the two-tailed exact Fisher test for unrelated groups. The differences at $p<0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

Table 1 presents a detailed general description of patients before the start of local treatment, divided into a group of vacuum therapy (group 1), collagen-containing dressings (group 2) and a control group (group 3).

As can be seen in Table 1, the patients assigned to a particular group were comparable in terms of sex, age, and state of carbohydrate metabolism. The patients examined were predominantly male.

Table 1. Characteristics of the examined patients before the start of local treatment of wounds.

Index	Group 1 NPWT (n=21)	Group 2 Collagen (n=21)	Group 3 Control (n=21)	p-value*	p-value**
Age, Me [Q25;Q75], years	60 [52;64]	55 [50;66]	60 [57;72]	0,26	0,16
Sex (m/f)	14/7	14/7	14/7	1,0	1,0
The duration of diabetes mellitus, Me [Q25;Q75], years	16 [12;24]	15 [13;16]	12 [9; 16]	39	0,19
Type 1 diabetes mellitus / type 2 diabetes mellitus	5/16	5/16	1/20	0,73	0,18
HbA 1c, Me [Q25;Q75],%	8,8 [7,4; 10,6]	8,3 [7,8; 9,5]	8,8 [7,6; 9,7]	0,83	0,63
P* - Group 1-3					
P** - Group 2-3					

Group 1 patients had a longer duration of diabetes mellitus. The average age of the patients was 58±11 years. Most of the patients assigned to different perioperative treatment groups suffered from type 2 diabetes mellitus. In patients with diabetes mellitus Type, 1 average duration of the disease was 21±6.8 years, in people with type 2 diabetes mellitus - 14±6.5 years. The median values of glycated haemoglobin (HbA1c) in all examined patients were 8.7% [7.6; 10], which indicates unsatisfactory control of the disease.

In all patients included in the study, the severity of microvascular complications of diabetes mellitus was

assessed: diabetic polyneuropathy, diabetic nephropathy, and diabetic retinopathy. The groups did not differ statistically in the severity of microvascular complications of diabetes mellitus. Almost all patients had distal diabetic polyneuropathy. According to the data presented, 3 patients did not have pronounced manifestations of neuropathy results of peripheral sensitivity assessment. However, the presence of dry skin and hyperkeratosis of the feet, as well as disruption of the sweat glands, made it possible to regard the above symptoms as the initial manifestations of peripheral innervation disorders. The groups differed slightly in the presence of non-proliferative retinopathy.

According to laboratory blood tests, the examined patients had no signs of an acute inflammatory process: the values of blood leukocytes corresponded to normal. The presence of anaemia and hypoproteinemia in the examined persons was not confirmed: haemoglobin and total blood protein indicators were within the reference limits for each category of patients. In all patients, the median glomerular filtration rate (MDRD) (Me[Q25; Q75]) was equal to 85 [62; 102], which corresponds to stage 2 of chronic renal failure against the background of diabetic nephropathy.

Thus, these factors are excluded as causes of delayed healing of wounds of the lower extremities in patients of the three groups. One of the leading factors in successful wound healing in diabetes mellitus is a sufficient supply of oxygen to tissues [24].

Because the exclusion criterion was the presence of critical ischemia of the lower limb, in all examined patients with the neuroischemic form of diabetic foot syndrome, the stable blood flow in the arteries of this area was determined according to Doppler and transcutaneous oximetry, there were no signs of critical ischemia of the affected limb. In group 1, tcpO2 was 46 [38; 52] mm Hg, in group 2 – 47 [41; 51], and in group 3 – 43 [38; 47]. There were no statistical differences between the groups (p1-3 = 0.29, p2-3 = 0.19).

All patients underwent surgical treatment of the wound defect, the required antibiotic therapy and unloading of the lower extremities. Antibacterial drugs were prescribed to prevent secondary infection of wounds, which is possible when changing dressings [12,38,41].

During the examination, it was found that all patients included in the study were comparable in the severity of reparative processes in the soft tissues of the lower extremities according to light microscopy and immunohistochemical analysis (p>0.05). In the wounds of the examined groups, there was pronounced oedema, a poorly organized extracellular matrix, low content of fibroblast-like cells and severe inflammatory infiltration, and the presence of young granulation tissue (p>0.05) was revealed. A detailed description of the morphological picture of wound biopsy specimens before treatment is presented in Table 2.

Table 2. Histological characteristics of the examined groups before the start of local treatment.

Histological characteristics	Group 1 NPWT (n=21)	Group 2 Collagen (n=21)	Group 3 Control (n=21)
Phase of the wound process, Me [Q25;Q75]	1 [1;1]	1 [1;2]	1 [1;2]
Severity of edema, Me [Q25;Q75]	3 [3;4]	3 [3;4]	4 [3;4]
Severity of the extracellular matrix, Me [Q25;Q75]	2 [1;2]	1 [1;2]	2 [1;2]
Maturity of granulation tissue, Me [Q25;Q75],%	1 [1;2]	1 [1;2]	1 [1;1]

Even though in many patients the course of the wound process was long and sometimes resistant to local treatment, the surgical treatment made it possible to translate the chronic process into an acute one. According to the results of the immunohistochemical study, a moderate number of macrophages (immunopositivity with antibodies to CD68), intense staining of matrix metalloprotease-9, weak staining of TIMP-1 and osteopontin (p>0.05) were initially noted in all groups (Table 3).

Table 3. The intensity of reparative processes according to immunohistochemical studies before the start of therapy

Repair marker	Group 1 NPWT (n=21)	Group 2 Collagen (n=21)	Group 3 Control (n=21)
Number of vessels during staining to CD31, Me [Q25;Q75]	46 [33;66]	43 [19;62]	58 [30;95]
Number of macrophages on staining to CD68, Me [Q25;Q75]	10 [10;15]	15 [5;20]	10 [5;15]
OPN, Median expression, Me [Q25;Q75]	3 [2;3]	3 [3;3]	3 [2;4]
MMP-9 Expression, Me [Q25;Q75]	3 [2;4]	4 [3;4]	4 [2;4]
TIMP-1 expression, Me [Q25;Q75]	1 [1;2]	1 [1;2]	2 [1;3]

Attention is drawn to the fact that in the current study, no correlation between glycated hemoglobin values and healing rate was revealed. In addition, the rest of the lab-

oratory parameters also did not affect the reparative processes of soft tissues.

According to the results of the treatment lasting 9±2 days, a significant difference in the dynamics of the area and depth of wounds during negative pressure therapy was revealed compared with standard therapy and when comparing the results of collagen therapy with standard treatment.

Even though the differences between the groups were not significant (p>0.05), there is a clear trend towards a more pronounced reduction in the wound area in the first group. The area of wounds decreased by 19.8% [10; 37.7] in group 1, by 26.4% [11.7; 32.4] in group 2, and by 17.0% [13.3; 26.7] in group 3.

The depth of wound defects during treatment decreased by 42.8% [24.3; 60.0] in the vacuum therapy group, by 30.4% [20.0; 41.1] in the collagen-containing dressings group, and by 16.6% [12.5; 32.2] in the control group. The differences between groups 1 and 2 with standard treatment are significant. Attention is drawn to the fact that negative pressure therapy more than effectively influenced the depth of wounds than the values of their area [16, 22, 32, 40]. While collagen therapy was most effective in reducing the area of wounds, but not the depth.

Thus, it can be concluded that both vacuum therapy and the use of collagen-containing dressings have a more effective effect on the clinical parameters of healing than standard topical treatment. Because negative pressure therapy effectively reduces the depth of wounds after surgical treatment and topical application of collagen improve the parameters of the area, it can be concluded that the use of a vacuum is a priority in patients with deep wound defects and abundant exudation [19].

During the examination, it was found that the median $tcpO_2$ in group 1 was 46 [38; 52] mm Hg, in group 2 – 47 [41; 51], and in group 3 – 43 [38; 47]. There were no statistical differences between the groups (p1-3=0.29, p2-3=0.19), which indicates a well-functioning arterial blood flow in the affected limb and the absence of critical ischemia in the examined [17].

Against the background of local treatment, a significant increase in the partial pressure of oxygen in group 1 was recorded: the median $tcpO_2$ after treatment was 52 mm Hg. [48;58] (initially - 46 [38; 52]), p<0.01, tcpO2 values in group 2 - 48 [45; 053] mm Hg. (Before treatment - 47 [41; 51] mm Hg), p - 0.18, in group 3 - 39 [32; 47], (before therapy - 43 [38; 47] mm Hg), p = 0.017. When comparing the results of the treatment of groups 1 and 2 with the control group, significant differences in the results obtained were revealed (p<0.001 and p=0.02, respectively).

Thus, we can say that negative pressure therapy significantly enhances local microcirculation. This significantly improves reparative processes, increases the rate of healing, and contributes to a more effective effect of drug therapy, since with the intensification of the local blood supply, the delivery of antibacterial drugs to the wound improves. Attention is drawn to a slight decrease in local microcirculation against the background of standard treatment, which may be due to the error of the method and the persistence of post-traumatic oedema in the surrounding tissues [35].

Pain syndrome in patients with chronic foot wounds is an extremely unfavourable healing factor [39]. It reduces both the quality of life of patients and their adherence to treatment and can lead to a slowdown in reparative processes. It should be noted that before the start of therapy in most patients, the pain syndrome was moderately expressed because of existing polyneuropathy. Against the background of treatment, regression of pain was recorded in all groups. A more pronounced downward trend was noted in the intensity of pain during negative pressure therapy and topical application of collagen compared to standard treatment (p<0.05). Of course, this may be a consequence of both a decrease in inflammation against the background of a complex of therapeutic measures and the direct influence of local treatment.

Interestingly, none of the patients included in the study refused to continue negative pressure therapy for one reason or another (inconvenience, noise, fear, etc.). This was facilitated by the absence of unpleasant pain against the background of local treatment. In addition, it is possible that the decrease in the intensity of pain syndrome against the background of vacuum therapy is due to a rarer, compared with other methods used, changing the dressing, as well as reducing the area of damaged tissues.

Against the background of topical application of collagen, a decrease in pain syndrome was also noted compared with standard therapy. During the histological examination of biopsy specimens of wound defects before treatment, it was found that all wounds were comparable in terms of the state of reparative processes in soft tissues. All patients had severe edema, poorly organized extracellular matrix, low content of fibroblast-like cells and significant inflammatory infiltrate (p>0.05). All wounds were in the phase of inflammation.

Against the background of treatment in groups 1 and 2, it was possible to achieve a more pronounced tenden-

cy to reduce intercellular edema compared to the control group, but the differences obtained were statistically insignificant. The dynamics of changes in the organization of the extracellular matrix because of one or another method of local treatment was not obtained. Perhaps this is due to the difficult assessment of this parameter when staining with hematoxylin-eosin.

According to light microscopy of biopsy specimens of wound defects in the groups of vacuum therapy and collagen-containing dressings, the transition of granulation tissue from young to mature was recorded, while in the control group, the granulation tissue had the character of maturing. However, against the background of negative pressure therapy, this transition was statistically reliable compared to the control group ($p<0.05$), and in the group of collagen-containing dressings, there were no differences from the control group ($p=0.28$). In addition, the data of the morphological picture demonstrate a significant process of transition of wounds from the phase of inflammation to the phase of epithelialization in all examined groups, however, there were no statistically significant differences between the groups.

The immunohistochemical study also showed a slowdown in reparative processes in the soft tissues of the lower extremities in the examined patients with diabetes mellitus, and a slowdown in neoangiogenesis before the start of therapy was recorded. When counting the number of vessels stained with the CD31 endothelial cell marker, a small number of vessels per unit area was noted. Thus, the average number of vessels in wound biopsy specimens before treatment was 57±43 per 1 mm, which also indicates a slowdown in the repair processes in the examined individuals before the start of local treatment.

In group 2, an increase in the number of vessels was also revealed: the median after treatment is 84 [50; 109] per unit area, which is also evidence of the transition of the wound process to the epithelialization phase.

In the control group, there was also an increase in the number of forming vessels: the median number after treatment was 97 [56; 157]. However, there were no significant differences between the groups.

During this study, it was found that the level of expression of osteopontin was reduced in most patients. Against the background of treatment, there is an increase in OPN expression in groups 1 and 2. When comparing the results obtained with the data of the control group, no statistically significant differences were obtained. In all groups, there was a tendency to increase the expression of this maker of healing, which is also a criterion for good wound healing. In all patients, staining of the CD68 macrophage marker was observed before treatment.

In laboratory models, it has been proven that in diabetes mellitus, the number of macrophages in the wound accumulates for a longer time, which may be associated with an increase in the level of pro-inflammatory cytokines and proteases and a reduced number of growth factors.

When comparing the results obtained, there are statistical differences between groups 1 and 3, $p = 0.01$, when comparing groups 2 and 3, no similar data were recorded: $p = 0.06$ Thus, it can be argued that vacuum therapy effectively affects the increase in the number of alternatively activated macrophages (judging by their phenotype), which is also an indicator of the transition of the wound process to the stage of remodelling.

Before treatment, an increase in the expression of MMP-9 and weak staining of TIMP-1 were recorded, which indicates high proteolytic activity in wounds and, according to some studies, leads to a slowdown in collagen restructuring and is an unsatisfactory prognostic sign of wound healing.

Against the background of treatment in all groups, there was a decrease in the expression of MMP-9 and an increase in the expression of TIMP-1.

In group 1, there was a significant decrease in MMP-9 ($p<0.01$) and an increase in TIMP-1 ($p=0.009$) during treatment. In group 2, a similar result was obtained: MMP-9 during collagen therapy decreased significantly ($p = 0.007$), despite the tendency to increase TIMP, the data were unreliable $p = 0.064$.

In the control group, MMP-9 expression also significantly decreased, $p = 0.018$, TIMP - without statistically significant dynamics: $p = 0.09$.

An analysis of the effect of concomitant diseases on the healing rate of wound defects was carried out.

As can be seen from Table 4, there were no significant differences in the healing processes in individuals without severe concomitant diseases and with their presence.

Table 4. Effect of the presence of comorbidities on healing outcomes.

Index	There are serious illnesses, n=35	There are no serious illnesses, n=28	p-value
The difference in wounds	18,6 [9,9;30,3]	26,2 [13,4;34,6]	0,116430
The difference in the depth of wounds	30,4 [16,6;54,5]	28,9 [15,7;40,9]	0,538207

There were no correlations between the values of glycated haemoglobin, as well as other laboratory blood parameters (haemoglobin, total protein, glomerular filtration rate) and the difference in depth and area against the background of all types of treatment. The correlation coefficient varies from -0.02 to 0.02. During correlation analysis, the effect of TIMP-1 activity on the depth of wounds was noted. So, with greater activity of this indicator against the background of treatment in all patients, the depth of the wounds was smaller, and the correlation coefficient r (according to Spearman) = -0.19. Attention is drawn to the correlation between MMP expression and the phase of the wound process, the correlation coefficient r (according to Spearman) = -0.21.

Thus, the highest expression of MMP was determined in the initial phases of the wound process, namely in the phase of inflammation. In addition, a correlation between the values of TIMP-1 and the severity of oedema, the correlation coefficient RS = -0.21 was recorded. The level of oedema depended on the values of TIMP-1: with an increase in the expression of this MMP inhibitor, the severity of oedema decreased.

Based on the analysis of the data obtained on the effect of each of the methods of local treatment of wounds on the clinical and cellular aspects of healing, an algorithm for managing patients with neuropathic and neuroischemic (without critical ischemia) forms of diabetic foot syndrome in the perioperative period is proposed. After the surgical treatment, it is necessary to assess the depth and area of the wound defect. If the postoperative wound is clean, there are no signs of inflammation and secondary necrosis, As well as the wound defect has a sufficient volume and exudation, the priority is the use of negative pressure therapy in order to more quickly form granulation tissue, reduce the size of the defect and prepare the wound for the next stage of treatment. If it is impossible to perform plastic closure with local tissues, it is recommended to maintain the wound in an open way until healing is achieved by secondary tension. In this case, the use of collagen-based dressings is indicated.

CONCLUSIONS

In patients with diabetes mellitus, reparative processes in soft tissues are slowed down, which is expressed in the presence of intercellular oedema, poor organization of the extracellular matrix, decreased expression of osteopontin and TIMP-1, and a reduced number of macrophages according to the results of histological and immunohistochemical studies. At the same time, negative pressure therapy and collagen-containing dressings effectively reduce both the area and depth of wound defects after primary surgical treatment compared to standard treatment ($p<0.05$) in patients with neuropathic and neuroischemic forms of diabetic foot syndrome. In turn, in Vacuum therapy significantly improves local microhemodynamics according to transcutaneous oximetry compared to standard therapy ($P<0.001$)

Negative pressure therapy and topical application of collagen significantly accelerate the reparative processes in the soft tissues of the lower extremities in individuals with diabetic foot syndrome compared to standard treatment, which is expressed in a reduction in the transition of the wound process from the phase of inflammation to the phase of epithelialization according to histological and immunohistochemical studies, which reveal a decrease in the number of inflammatory infiltrate cells, a decrease in edema and organization extracellular matrix and the formation of mature granulation tissue, as well as an increase in the expression of the macrophage marker CD68 and osteopontin. The successful process of wound healing in diabetic foot syndrome is characterized by an increase in the number of newly formed vessels ($p<0.05$). Local use of negative pressure and collagen leads to a significant ($p<0.05$) decrease in the level of expression of matrix metalloprotease-9 and a tendency to increase the synthesis of tissue inhibitor metalloprotease - 1, which leads to an acceleration of the organization of the extracellular matrix and the formation of high-quality granulation tissue.

We believe that modern methods of local treatment (negative pressure therapy, collagen-containing dressings) after the initial surgical treatment of chronic wounds should be used differentially depending on the volume of the wound and the amount of exudate. This will significantly improve the therapeutic prognosis and shorten the treatment time. The algorithm for managing patients with wound defects of the feet after surgical treatment, including an assessment of the condition of the wound, the amount and nature of the exudate, and the transcutaneous oxygen tension of the tissues, will optimize the treatment process and significantly reduce the length of the patient's stay in the hospital. The determination of immunohistochemical markers such as CD31, CD68, osteopontin, as well as MMP-9 and TIMP-1 makes it possible to accurately assess the intensity of reparative processes in soft tissues in individuals with various forms of diabetic foot syndrome and can be recommended as a model for assessing the severity of repair in clinical trials. Enhancement of local microhemody-

namics according to transcutaneous oximetry against the background of treatment is a predictor of good wound healing and is recommended for widespread use.

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REFERENCES:

1. Bolton L. Diabetic foot ulcer: treatment challenges. // Wounds. - 2022 Jun;34(6):175-177. doi: 10.25270/wnds/2022.175177. PMID: 35881427.
2. Borys S., Hohendorff J., Frankfurter C., et al. Negative pressure wound therapy use in diabetic foot syndrome-from mechanisms of action to clinical practice. // Eur. J. Clin. Invest. - 2019 Apr;49(4):e13067. doi: 10.1111/eci.13067. Epub 2019 Jan 29. PMID: 30600541.
3. Donath M.Y., Dinarello C.A., Mandrup-Poulsen T. Targeting innate immune mediators in type 1 and type 2 diabetes. // Nat. Rev. Immunol. - 2019 Dec;19(12):734-746. doi: 10.1038/s41577-019-0213-9. Epub 2019 Sep 9. PMID: 31501536.
4. Firdous S., Wagai G.A., Sharma K. A survey on diabetes risk prediction using machine learning approaches. // J. Family Med. Prim. Care. - 2022 Nov;11(11):6929-6934. doi: 10.4103/jfmpc.jfmpc_502_22. Epub 2022 Dec 16. PMID: 36993028; PMCID: PMC10041290.
5. Góralczyk K., Szymańska J., Gryko Ł., et al. Low-level laser irradiation modifies the effect of hyperglycemia on adhesion molecule levels. // Lasers Med. Sci. - 2018 Sep;33(7):1521-1526. doi: 10.1007/s10103-018-2511-z. Epub 2018 May 3. PMID: 29725945.
6. Götz J., Lange M., Dullien S., et al. Off-loading strategies in diabetic foot syndrome-evaluation of different devices. // Int. Orthop. - 2017 Feb;41(2):239-246. doi: 10.1007/s00264-016-3358-1. Epub 2016 Dec 9. PMID: 27942889.
7. Krivoshchekov E.P., El'shin E.B., Romanov V.E., et al. Puti sokhraneniia konechnosti v posleoperatsionnom periode lecheniia oslozhneniĭ sindroma diabeticheskoĭ stopy [Ways of limbs salvage in postoperative period of treatment of complications of diabetic foot syndrome]. // Angiol. Sosud. Khir. - 2020;26(4):33-41. Russian. doi: 10.33529/ANGIO2020401. PMID: 33332304.
8. Kulwas A., Drela E., Jundziłł W., et al. Circulating endothelial progenitor cells and angiogenic factors in diabetes-complicated diabetic foot and without foot complications. // J. Diabetes Complications. - 2015 Jul;29(5):686-90. doi: 10.1016/j.jdiacomp.2015.03.013. Epub 2015 Apr 6. PMID: 25872462.
9. Lipsky B.A., Berendt A.R., Cornia P.B., et al. Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. // Clin. Infect. Dis. - 2012 Jun;54(12):e132-73. doi: 10.1093/cid/cis346. PMID: 22619242.
10. Němcová A., Dubský M., Jirkovská A., et al. Syndrom diabetické nohy: význam MR spektroskopie lýtkových svalů pro hodnocení končetinové ischemie a efektu revaskularizace [Diabetic foot syndrome: importance of calf muscles MR spectroscopy in the assessment of limb ischemia and effect of revascularization]. // Vnitr Lek. - 2017 Spring;63(4):236-241. Czech. PMID: 28520446.
11. Noor S., Khan R.U., Ahmad J. Understanding Diabetic Foot Infection and its Management. // Diabetes. Metab. Syndr. - 2017 Apr-Jun;11(2):149-156. doi: 10.1016/j.dsx.2016.06.023. Epub 2016 Jun 18. PMID: 27377687.
12. Normandin S., Safran T., Winocour S., et al. Negative Pressure Wound Therapy: Mechanism of Action and Clinical Applications. // Semin. Plast. Surg. - 2021 Aug;35(3):164-170. doi: 10.1055/s-0041-1731792. Epub 2021 Sep 10. PMID: 34526864; PMCID: PMC8432996.
13. Petersen K.S., Clifton P.M., Blanch N., et al. Effect of improving dietary quality on carotid intima-media thickness in subjects with type 1 and type 2 diabetes: a 12-mo randomized controlled trial. // Am. J. Clin. Nutr. - 2015 Oct;102(4):771-9. doi: 10.3945/ajcn.115.112151. Epub 2015 Sep 9. PMID: 26354542.

14. Pitocco D., Spanu T., Di Leo M., et al. Diabetic foot infections: a comprehensive overview. // Eur. Rev. Med. Pharmacol. Sci. - 2019 Apr;23(2 Suppl):26-37. doi: 10.26355/eurrev_201904_17471. PMID: 30977868.
15. Rdeini W.M., Agbenorku P., Mitish V.A. Strategy of surgical management of peripheral neuropathy form of diabetic foot syndrome in ghana. // Plast. Surg. Int. - 2014;2014:185023. doi: 10.1155/2014/185023. Epub 2014 Jul 24. PMID: 25152815; PMCID: PMC4131423.
16. Ruszkowska-Ciastek B., Sokup A., Socha M.W., et al. A preliminary evaluation of VEGF-A, VEGFR1 and VEGFR2 in patients with well-controlled type 2 diabetes mellitus. // J. Zhejiang. Univ. Sci B. - 2014 Jun;15(6):575-81. doi: 10.1631/jzus.B1400024. PMID: 24903995; PMCID: PMC4116851.
17. Shi Y., Vanhoutte P.M. Macro- and microvascular endothelial dysfunction in diabetes. // J. Diabetes. - 2017 May;9(5):434-449. doi: 10.1111/1753-0407.12521. Epub 2017 Mar 1. PMID: 28044409.
18. Szabad G. A diabeteses láb [Diabetic foot syndrome]. // Orv Hetil. - 2011 Jul 17;152(29):1171-7. Hungarian. doi: 10.1556/OH.2011.29168. PMID: 21712183.
19. You M., Liu Y., Wang B., et al. Asprosin induces vascular endothelial-to-mesenchymal transition in diabetic lower extremity peripheral artery disease. // Cardiovasc. Diabetol. - 2022 Feb 15;21(1):25. doi: 10.1186/s12933-022-01457-0. PMID: 35168605; PMCID: PMC8848671.
20. Záhumenský E. Infekce a syndrom diabetické nohy v terénní praxi [Infections and diabetic foot syndrome in-field practice]. // Vnitr Lek. - 2006 May;52(5):411-6. Czech. PMID: 16771079.
21. Zubair M., Ahmad J. Role of growth factors and cytokines in diabetic foot ulcer healing: A detailed review. // Rev. Endocr. Metab. Disord. - 2019 Jun;20(2):207-217. doi: 10.1007/s11154-019-09492-1. PMID: 30937614.
22. Okhunov A. Influence of a granulocyte-colony-stimulating factor on the cytological picture of the wound in patients with purulent-inflammatory diseases of soft tissues on the background of diabetes mellitus. Research Square; 2022. DOI: 10.21203/rs.3.rs-2304237/v1.
23. Okhunov A. O. The role and place of nitroxidergic regulation of the endothelial system in the pathogenesis of acute lung abscess. // Medical & Clinical Research 7.12 (2022): P. 1-6.
24. Okhunov A. O., Abdurakhmanov F. M. Ways to achieve positive results of dermaplasty in patients with diabetic foot syndrome. // British Medical Journal 3.1 (2023).
25. Okhunov A. O., Boboev Q. Kh., Valijonov A. Principles of diagnosis and treatment of acute purulent-destructive lung diseases. // World Bulletin of Public Health, 2022, #7, P. 1-2. Retrieved from https://scholarexpress.net/index.php/wbph/article/view/526
26. Okhunov A. O., Bobokulova Sh. A. Differentiated approaches to the diagnosis and treatment of acute lung abscesses in patients who have had COVID-19. // British Medical Journal, 2023, # 3.1.
27. Okhunov A. O., Khamdamov Sh A. Evaluation of the effectiveness of various methods of treatment of acute purulent-destructive lung diseases in patients with diabetes mellitus. // British Medical Journal, 2023, # 3.2.
28. Okhunov A. O., Khamdamov Sh. A. A combination of diabetes mellitus and acute purulent-destructive lung diseases solving the problems of diagnosis and treatment. // World Bulletin of Public Health, 2023, #19, P. 127-135. Retrieved from https://scholarexpress.net/index.php/wbph/article/view/2149
29. Okhunov A. O., Korikhonov D. N. Differential diagnosis of necrotizing fasciitis. // British Medical Journal, 2023, # 3.1.
30. Okhunov A.O, Bobokulova Sh. A. New approaches to treating lung abscesses as covid19 sequels. // World Bulletin of Public Health, 2023, #19, P. 101-107. Retrieved from https://scholarexpress.net/index.php/wbph/article/view/2281
31. Okhunov A.O. Endovascular methods for correcting angiopathy of the diabetic foot syndrome in patients after COVID-19 // 16th European Diabetes and Endocrinology Congress – 2022, P.12-15.
32. Okhunov A.O. Endovascular methods for correcting angiopathy of the diabetic foot syndrome in patients after COVID-19. // 16th European Diabetes and Endocrinology Congress. – 2022. – P.12-15.
33. Okhunov A.O. Postoperative complications issues after the application of various abdominoplasty techniques. // 4-international conference of the European Academy of Science. – 2019. – P.23-24.
34. Okhunov A.O. Prediction and prevention of sepsis in patients with necrotizing fasciitis on the background of diabetes mellitus // 42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA, 2023, April 11-14, P.39.
35. Okhunov A.O. Prediction and prevention of sepsis in patients with necrotizing fasciitis on the background of diabetes mellitus. // Conference «42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA April 11-14, 2023» - P.39.

36. Okhunov A.O., Abdurakhmanov F.A. Prolonged intraarterial catheter therapy for diabetic gangrene of the lower limb. // Conference «42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA April 11-14, 2023» - P.38.
37. Okhunov A.O., Abduralhmanov F.M. Prolonged intraarterial catheter therapy for diabetic gangrene of the lower limb // 42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA April 11-14, 2023 – P.38
38. Okhunov A.O., Boboev K.Kh. Etiological factors leading to purulent mediastinitis. // World Bulletin of Public Health, 2023, #18, P. 118-125.
39. Okhunov A.O., Boboev K.Kh. Etiology and pathogenesis of primary purulent mediastinitis. // British Medical Journal, 2023, #3.1.
40. Oxunov A.O., Babadjanov B.D., Pulatov U.I. Sepsis. - Patent RUz DGU 04057 ot 13.10.2016 g. [in Russian].
41. Oxunov A.O., Pulatov U.I., Oxunova D.A. Morfologicheskaya xarakteristika techeniya ranevogo protsessa pri gnoyno-vospalitelnix zabolevaniyax myagkix tkaney na fone saxarnogo diabeta. // Vestnik nauki i obrazovaniya. – 2018. - №9 (45). – S.98-104. [in Russian].
42. Principles of Diagnosis and Treatment of Acute purulent-destructive lung diseases. / A.O. Okhunov, K.X. Boboev, A.F. Valijonov, et al. // World Bulletin of Public Health. – 2022. – Vol.7. – P.1-2.
43. Puti uluchsheniya rezultatov lecheniya bolьnыx s gnoynovospalitelnыmi porajeniyami myagkix tkaney na fone saxarnogo diabeta. / A.O. Oxunov, U.I. Pulatov, B.D. Babadjanov, et al. // TAJRIR JAYATI. - 2012. - S.82. [in Russian].
44. Sayfullaeva S.A. Aktivnost monooksigenaznoy i nitrergicheskoy sistem v mikrosomax pecheni pri deystvii na organizm induktorov i ingibitorov lekarstvennogo metabolizma // Vrach-aspirant. - 2013. - Tom 59. - №4. - S.73-78. [in Russian].
45. Sayfullaeva S.A. Metabolicheskaya aktivnost mikrosom slizistoy obolochki kulti jeludka posle rezektsii porajennogo yazvennim protsessom uchastka gastroduodenalnoy zone // Vrach-aspirant - 2010. - Tom. 39. - №2.1. - S.131-140. [in Russian].
46. Shadmanov A.K. A new method of treating pneumonia complicated by an abscess in patients after Covid-19. // Journal of Education and Scientific Medicine. – 2023. – Vol.1. - #2. – P.2-9.
47. Shadmanov A.K. Features of the Educational Program in Foreign Universities: The Example of the Medical College of the University of Central Florida // Journal of Education and Scientific Medicine. – 2023. – Vol.2. - #2. – P.2-9.
48. The microbiological environment of wounds and skin in patients with purulent-inflammatory diseases of soft tissues. / W.S. Jonson, A.O. Okhunov, S.S. Atakov, et al. // Journal of Education and Scientific Medicine. – 2023. – Vol.2. - #2. – P.72-81.

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DIABETIK OYOQ SINDROMI DAVOLASHDA KLINIK VA MORFOLOGIK ASOSLARI

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ABSTRAKT

Dolzarbligi: Odatda, klinik amaliyotda faqat shakl beruvchi granulyatsiya to'qimasining tashqi xususiyatlari baholanadi. Bunday to'qimalar yetarli emas va davolashda xatoliklarga olib kelishi mumkin. Granulyatsiya etukligining morfologik xususiyatlari uglevod metabolizmi buzilishlarisiz laboratoriya modellarida yoki shaxslarda baholandi.

Tadqiqot: Parallel guruhlar, jumladan, qandli diabet va diabetik oyoq sindromi bilan og'rilgan bemorlar bilan ochiq bo'lajak, tasodifiy solishtirma tadqiqot dizaynida o'tkazildi. Umumiy klinik, biokimyoviy, instrumental, funksional, morfologik, immunologik, histokimyoviy va statistik tadqiqot usullari amalga oshirildi.

Natijalar: Surunkali yaralarni birlamchi jarrohlik davolashdan so'ng mahalliy davolashning zamonaviy usullari yaraning miqdori va ekssudat miqdoriga qarab differentsial tarzda qo'llanilishi kerak. Bu terapevtik prognozni sezilarli darajada yaxshilaydi va davolanish muddatini qisqartiradi. Davolash jarayonining optimallashuvi qayd etilib, bemorning shifoxonada qolish davri sezilarli darajada qisqartirildi. Reparativ jarayonlarning intensivligi CD31, CD68, osteopontin kabi immunohistokimyoviy belgilarini, matritsali metalloproteazlarning ktivatsiyasini va metalloproteazlarning to'qima inhibitorini aniqlash orqali baholanishi mumkin. Yaxshi yara shifo ishonchli bashoratchisi sifatida transkutan oksimetriyaga ko'ra mahalliy mikrohemodynamika ko'payadi.

Hulosa: pastki ekstremitalarning yumshoq to'qimalarida reparativ jarayonlar diabet bilan og'rigan shaxslarda buziladi. Yaralarni mahalliy davolashning turli turlari qandli diabet bilan og'rayotgan bemorlarda shifobaxsh jarayonlarning intensivligiga turli ta'sir ko'rsatishi mumkin. Mavzuli davolash turi yarani o'rab turgan to'qimalarda mahalliy mikrohemodinamikaga ta'sir qilishi mumkin.

Tayanch iboralar: Qandli diabet, diabetik oyoq sindromi, yaraning regeneratsiyasi

КЛИНИКО-МОРФОЛОГИЧЕСКОЕ ОБОСНОВАНИЕ ВЫБОРА МЕТОДА ЛЕЧЕНИЯ ИЛИ СИНДРОМА ДИАБЕТИЧЕСКОЙ СТОПЫ

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АБСТРАКТ.

Актуальность: Обычно в клинической практике оценивают только внешние характеристики формирующейся грануляционной ткани, что является недостаточным и может привести к ошибкам в лечении. Морфологические характеристики грануляционной зрелости оценивали на лабораторных моделях или у лиц без нарушений углеводного обмена.

Материал и методы: Исследование проводилось в дизайне открытого проспективного рандомизированного сравнительного исследования с параллельными группами, включающими пациентов с сахарным диабетом и синдромом диабетической стопы. Проведены общеклинические, биохимические, инструментальные, функциональные, морфологические, иммунологические, гистохимические и статистические методы исследования.

Результаты: Современные методы местного лечения после первичной хирургической обработки хронических ран следует применять дифференцированно в зависимости от объема раны и количества экссудата. Это значительно улучшит терапевтический прогноз и сократит продолжительность лечения. Отмечена оптимизация лечебного процесса, а также значительно сокращен срок пребывания пациента в стационаре. Интенсивность репаративных процессов можно оценить по определению иммуногистохимических маркеров, таких как CD31, CD68, остеопонтин, активность матриксных металлопротеаз и тканевый ингибитор металлопротеаз. В качестве надежного предиктора хорошего заживления ран отмечается увеличение локальной микрогемодинамики по данным чрескожной оксиметрии.

Выводы: Репаративные процессы в мягких тканях нижних конечностей нарушены у лиц с сахарным диабетом. Различные виды местного лечения ран по-разному влияют на интенсивность процессов заживления у больных сахарным диабетом. Тип местного лечения может влиять на местную микрогемодинамику в тканях, окружающих рану.

Ключевые слова: сахарный диабет, синдром диабетической стопы, регенерация ран